

### REMARKS

Claims 16 and 18-29 have been canceled merely in order to expedite prosecution of the present application. Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications.

Claim 6 has been rewritten as an independent claim. Claims 1-3 and 5-15 are pending. No new matter has been added.

#### ***Rejections Under 35 U.S.C. § 112, First Paragraph***

Claims 1-3, 5-16 and 18-29 are rejected as allegedly not being enabled. The Office Action asserts that the claims "cover all compounds having the pharmaceutical property of being known descriptively as a specific inhibitor of PKC. Accordingly, the instant specification only provides guidance and support for the bisindolylmaleimide compounds." The Office Action concludes that "one skilled in the art is subjected to an undue experimentation in order to determine the other compounds which are supported by the pharmaceutical property of being known as specific PKC inhibitors." This rejection is respectfully traversed, for at least the following reasons.

At the time of filing, numerous PKC inhibitors were known that could be used in the presently claimed compounds and methods. See, for example, Goekjian et al. (1999) Protein Kinase C in the Treatment of Disease: Signal Transduction Pathways, Inhibitors, and Agents in Development. *Current Medicinal Chemistry* 6:877-903 (copy enclosed), and references cited therein, which demonstrate the state of the art at the time the instant application was filed.<sup>1</sup> As discussed in this article (see, e.g., pages 889-891 of Goekjian), several classes of selective PKC inhibitors were known in addition to bisindolylmaleimide compounds, for example, indolocarbazoles (such as CGP41251, Go 6976, Go 7612 and Go7874), balanoids (e.g., SPC 100840) and phenylamino-pyrimidine compounds (e.g., CGP53506). Other specific PKC

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<sup>1</sup> Although Goekjian was published in September of 1999, approximately six months after Applicant's priority date, Goekjian is a review article that almost exclusively cites and discusses references published prior to Applicant's March 12, 1999 priority date. Accordingly, Goekjian reflects the state of the art as of the priority date.

inhibitors known at the time of filing (and that could be used in vivo) include GF109203x (discussed at page 895 of Goekjian), RO32-0432 (discussed at page 896 of Goekjian), and CPR 1006 (discussed at page 897 of Goekjian). A skilled artisan could choose any one of these inhibitors to use in the claimed compositions and methods. Thus, given the high level of knowledge and skill in the relevant art, an ordinary artisan would clearly not need to perform undue experimentation in order to make and use the full scope of the present invention.

Moreover, as the Examiner is aware, the law does not require an applicant to describe in his specification every conceivable embodiment of the invention. It is sufficient that one embodiment is disclosed if other embodiments can be determined without undue experimentation. (See U.S. v. Teletronics, Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989), holding that since one embodiment and the method to determine other embodiments were set forth in the specification, the specification was enabling, regardless of the great time and expense involved in such determination). Applicants' specification clearly meets this standard. Furthermore, as stated in MPEP 2164.02, "[t]he presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure... To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims." MPEP 2164.02 goes on to say, "[p]roof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation." Such evidence has not been provided here. Particularly in view of the numerous PKC inhibitors known at the priority date, the identification of compounds within the scope of the claims requires (at most) routine experimentation.

Applicants note that claim 6 has been rewritten as an independent claim. As amended, claim 6 corresponds with the Examiner's acknowledged scope of enablement. Since claims 1-15 are indicated by the Examiner to be free of prior art, claim 6 and dependent claims 7 and 8 are allowable. Claims 16 and 18-29 have been canceled, although their rejection on enablement grounds is traversed for the reasons above.

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***Rejections Under 35 U.S.C. § 103***

Claims 16 and 18-29 remain rejected as unpatentable over Sitter et al. in view of Hu et al. This rejection is traversed for the reasons previously set forth. However, in order to expedite prosecution, claims 16 and 18-29 have been canceled. Applicants reserve the right to pursue these claims in a continuation application.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant submits that all claims are in condition for allowance. Enclosed is a Petition for Extension of Time with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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**Version with markings to show changes made**

**In the claims:**

Claims 16 and 18-29 have been cancelled.

Claim 6 has been amended as follows:

6. (Amended) A method of treating permeability failure in a subject, comprising:  
introducing into said subject a peritoneal dialysis fluid which includes [The method of claim  
2, wherein said inhibitor is] a bis (indolyl) maleimide protein kinase C (PKC) inhibitor,  
thereby treating said subject.